

Amendments to the Specification

Please replace the paragraph beginning at page 10, line 24 with the following amended paragraph:

The present invention also relates to the discovery that asthmatic individual heterozygous or homozygous for a 5-LO allele comprising the 5lo01a polymorphism have significantly decreased eosinophil levels as compared to related family members having no such allele. While not intending to be bound by any specific theory, the association between the 5lo01a polymorphism and reduced eosinophil levels may be explained by recent studies that showed that some metabolites of 5-LO can induce production of eosinophils (Urasaki, *et al.* (2001) *J. Leukocyte Biol.* 69(1):105-112 and Powell *et al.*, (2001) *J. Allergy. Clin. Immunol.* 107(2):272-278). Specifically, where an allele comprises the 5lo01a polymorphism, the allele also necessarily comprises the haplotype of the invention and a variant Sp1 binding site. 5-LO alleles comprising a variant Sp1 binding site have reduced levels of 5-LO expression which, in turn, result in reduced levels of 5-LO metabolites, thereby ultimately resulting in a reduction in the number of activated eosinophils. Thus, the presence of the haplotype or one or more polymorphisms comprising the haplotype can be used to predict whether a patient has a greater chance of having abnormally low eosinophil count. Eosinophil counts are used as an index of asthmatic disease, and reflect an asthma-related phenotype (see, for example, Jatakanon, A., *et al.* (2000) *Am. J. Respir. Crit. Care Med.* 161(1):64; Kamfar, *et al.* (1999) *J. Asthma* 36(2):153; and Lonnkvist, K. *et al.* (2001) *J. Allergy Clin. Immunol.* 107(5):812). High eosinophil counts in asthma patients are associated with a more severe asthma phenotype as compared to the asthma phenotype in asthma patients having low eosinophil counts. Accordingly, determination of any polymorphism comprising the haplotype of the invention can be used to predict whether an asthma patient has or will have a moderate disease phenotype. Moreover, determination of any polymorphism comprising the haplotype can be used to differentiate among asthmatic populations to those having a moderate disease phenotype and those having a relatively more severe disease phenotype. A disease phenotype, *e.g.*, the asthma phenotype, may be defined by established clinical parameters (see, for example, Moffitt *et al.* (1994) *Am. Fam. Phys.* 50:1039).

Please replace the paragraph beginning at page 12, line 26 with the following amended paragraph:

There are multiple alleles of the 5-LO gene. The reference 5-LO gene sequence designated herein is presumed to be the wild-type 5-LO gene sequence and comprises nucleotide sequences that have been deposited in ~~GenBank™~~ GENBANK™ and assigned the Accession Number GI 187166, GI 8247778, and GI 4502056 (corresponding to SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively). The present invention relates to variant alleles of the 5-LO gene that differ from the reference 5-LO gene sequence by at least one of the polymorphisms identified in Table 1, and those in linkage equilibrium therewith. The present invention thus relates to nucleic acids comprising such variant 5-LO alleles.

Please replace the paragraph beginning at page 66, line 8 with the following amended paragraph:

The amplified genomic DNA fragments were then analyzed by SSCP (Orita *et al.* (1989) *PNAS USA* 86:2766, see also Cotton (1993) *Mutat Res* 285:125-144; and Hayashi (1992) *Genet Anal Tech Appl* 9:73-79). From each 25 µl PCR reaction, 3 µl was taken and added to 7 µl of loading buffer. The mixture was heated to 94°C for 5 min and then immediately cooled in a slurry of ice-water. 3-4 µl were then loaded on a 10% polyacrylamide gel either with 10% glycerol or without 10% glycerol, and then subjected to electrophoresis either overnight at 4 Watts at room temperature, overnight at 4 Watts at 4°C (for amplifying a 5' upstream regulatory element), or for 5 hours at 20 Watts at 4°C. The secondary structure of single-stranded nucleic acids varies according to sequence, thus allowing the detection of small differences in nucleic acid sequence between similar nucleic acids. At the end of the electrophoretic period, the DNA was analyzed by gently overlaying a mixture of dyes onto the gel (1x the manufacturer's recommended concentration of ~~SYBR Green I™~~ SYBR GREEN I™ and ~~SYBR Green II™~~ SYBR GREEN II™ in 0.5 X TBE buffer (~~Molecular Probes™~~ MOLECULAR PROBES™)) for 5 min, followed by rinsing in distilled water and detection in a ~~Fluoroimager 575™~~ FLUOROIMAGER 575™ (~~Molecular Dynamics™~~ MOLECULAR DYNAMICS™).